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Evaluation of clinical and laboratory parameters in patients with influenza pneumonia

Clinic of patients with influenza pneumonia

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Abstract

Aim: In this study, we aimed to evaluate clinical and laboratory parameters of the cases diagnosed as influenza pneumonia. Material and Method: The files of the patients treated for confirmed influenza pneumonia either following hospitalization or on an outpatient basis between January 2015 and January 2017 in our hospital were retrospectively evaluated. The cases in whom influenza diagnosis had been confirmed by using multiplex PCR method in samples of nasopharyngeal swabs, sputum or bronchoalveolar lavage fluid were included in the study. Results: Thirty cases of pneumonia with confirmed influenza diagnosis were identified during the mentioned period. 70% of the cases were typed as influenza type A and 30% as influenza type B. The most frequently encountered symptoms were fever (70%) and cough (66.7%). Comorbidities were present in 76.7% of the cases. Medical history of the cases revealed diabetes mellitus (30%), hematologic malignancies (23.3%), and cardiovascular disorders (20%). Radiologic assessment was made in 93.3% of the cases and in 56.7% of them, infiltrations were identified in chest X-ray. CRP level was statistically significantly increased in cases with identified infiltration (p: 0.015). Discussion: Influenza pneumonia probability should not be overlooked when fever and cough symptoms are present in cases having chronic cardiopulmonary comorbidity and clinical conditions in which immune system has been affected during the influenza season. Immunization should be considered and recommended in this patient group. Although radiological evaluation is not necessary in every influenza case, radiologic imaging might be required in patients having a clinical course with elevated CRP levels.

Keywords

Influenza; Fever; Cough; CRP

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Introduction

Influenza is an acute viral infectious disease accompanied by fever, cough, headache, malaise, and rarely nausea, vomiting, and diarrhea. The virus causing the disease has many subtypes. Among these viruses belonging to Orthomyxoviridae family, the types named influenza A, B, and C lead to infection in humans. Influenza type A virus causes a pandemic, epidemic, or seasonal outbreaks, whereas influenza type B virus leads to the epidemic and seasonal outbreaks. Type C causes mild upper respiratory tract disorders, not causing an epidemic. Influenza type A virus leads to increased morbidity and mortality when compared to type B virus [1-5].

Influenza viruses can pass from person to person by aerosol droplets. Therefore, their contagiousness is increased. It has been reported that approximately 20% of the population in the USA can be infected by influenza every year (6-8). The influenza virus can cause upper or lower respiratory tract infections by adhering to the airway epithelium. The disease is usually self-limited and does not lead to severe clinical features; however, it might have a severe clinical course in patients under 2 or over 65 years of age, in the presence of a chronic disorder, immune suppression, or pregnancy [9-11]. The Centers for Disease Control and Prevention (CDC) estimates that influenza leads to 200.000 hospital admissions and a mortality ranging between 3.000-49.000 due to pneumonia every year in the USA [12].

Since it is a common disease, influenza creates a significant health burden. It is in the first place among the respiratory viral infections leading to hospitalization over the age of 16 years [13]. The labor loss and the expenditures due to the disease cause economic losses. Permanent immunity response does not occur even when the infection has been encountered because of the antigenic drifts occurring in the structure of the virus. Thus, the most effective method for the prevention of infections with influenza virus is an annual vaccination for influenza [14-15]. The priority should be given particularly to immunization of patients in whom the immune system is affected, such as diabetes mellitus (DM), cardiopulmonary disorders, chronic renal failure, hematologic malignancies, oncologic diseases, together with the risk groups such as elderly and pediatric populations.

In the light of this information, it was aimed to determine the clinical and laboratory features of the patients who had undergone treatment with the diagnosis of influenza pneumonia within the last two years in our hospital, functioning as a tertiary healthcare institution in our district.

Material and Methods

This study was performed according to the guidelines of the Helsinki Declaration and was approved by the local ethics committees of the Adnan Menderes University in Aydin, Turkey. The adult patients followed up by Pulmonology Department in Adnan Menderes University either with hospitalization or on an outpatient basis from January 2015 to January 2017 were evaluated. In these patients, the diagnosis had been made by multiplex real-time PCR analysis of the obtained nasopharyngeal swab, bronchoalveolar lavage, or sputum samples in patients having symptoms and findings of lower respiratory tract infection or radiologically identified infiltrations including consolidation or interstitial opacities. Specimens were studied by Respiratory 21 (FTD) (Fast-Track diagnostics, Junglinster, Luxembourg) kit. The files of the cases with the confirmed diagnosis of influenza were retrospectively investigated. The demographic, clinical, and laboratory data including leukocyte, neutrophil, and lymphocyte counts, neutrophil/lymphocyte ratio, and C-reactive protein (CRP) of the patients at the time of admission were recorded. Patients with bacterial or fungal agent in sputum or blood culture and patients who received antibiotic treatment were not included in the study.

Statistical Analysis

For the statistical analysis of the data obtained in the study, SPSS (Statistical Package for Social Sciences) for Windows 13.0 software was used. In this evaluation, for analysis of the quantitative data, "Mann-Whitney U test" was used for intergroup comparisons of the parameters having a non-normal distribution, in addition to the descriptive statistical methods (mean, standard deviation). $P<0.05$ was considered statistically significant.

Results

Thirty cases of influenza with a mean age of 58.06±19.08 years were identified at the specified period. No significant difference was present between female (53.3%) and male (46.7%) patients regarding the mean age. The mean ages of cases with influenza type A and B were 56.7 and 62.6 years, respectively. Of the cases, 70% had influenza type A, and 30% had influenza type B viruses. Fever (70%) and cough (66.7%) were the most frequently encountered symptoms (**Table 1**). In cases of influenza A, the most commonly identified complaints were fever (71.4%), cough (66.6%) and malaise (61.9%). In cases of influenza B, the most common complaints were fever (66.6%), cough (66.6%) and malaise (55.5%). Comorbidity was present in 76.7% and absent in 23.3% of the cases. When compared according to the influenza types, 14.2% of the influenza A cases and 44.4% of the influenza B cases had no additional disease. Within the whole patient group, the most common comorbidities were DM (29.2%), hematologic malignancies (23.3%), and cardiovascular diseases (20%) (**Table 2**). In influenza A cases, the rates of hematologic malignancies and DM were 28.5% and 23.8%, respectively. In influenza B cases, hematologic malignancy rate was 11.1%, whereas DM rate was 44.4%. When

Table 1. The most frequently encountered symptoms in our cases and their frequencies

Symptom	Number of cases (n)	Percentage (%)
Fever	21	70
Cough	20	66.7
Malaise	16	53.3
Sputum	8	26.7
Dyspnea	8	26.7
Sore throat	7	23.3
Somatic pain	7	23.3
Nausea-Vomiting	5	16,7
Diarrhea	3	10

Table 2. The accompanying diseases and their frequencies in the case group involved in the study

Accompanying disease	Number of cases (n)	Percentage (%)
Absent	7	23.3
Diabetes mellitus	9	29.2
Hematologic malignancy	7	23.3
Cardiovascular disorder (CAD, HT)	6	20
Renal failure	3	10
COPD	2	6.6

all cases were evaluated together, radiologic infiltration was present in 56.7% of the cases, whereas 36.7 did not have any infiltration. A radiologic evaluation was not performed at the time of diagnosis in 6.7% of the group. The rates of radiologic presence of infiltration were similar in influenza A and B groups (57.8% in influenza A, and 66.6% in influenza B, p=0.493). Moreover, the rates of radiologic infiltration in the groups with and without disorders that affect the immune system, such as DM and malignancies, were similar (66.6% and 53.8%, in the groups with and without affected immune system, respectively, p=0.488). In our study, the relationships of the radiologic presence of infiltration with leukocyte, neutrophil, and lymphocyte counts, neutrophil/lymphocyte ratio, and CRP level were also investigated. The only statistically significant relationship was found to be present with CRP level among all parameters (p= 0.015) (Table 3). Kendall correlation analysis revealed a positive correlation between CRP level and the presence of radiologic infiltration (r=0.389, p= 0.015).

Table 3. The comparison of the parameters in cases grouped according to the presence of inflammation in chest X-ray

	İnfiltration present n=17	İnfiltration absent n=11	p value
Hemoglobin	11.1(5.2-16.5)	12.5(8.8-16.1)	0.3
Leukocyte	7520(780-22680)	6920(660-14940)	0.572
Neutrophil	6000(230-21100)	3810(10-10350)	0.115
Lymphocyte	1030(340-4000)	1050(360-2920)	0.621
Neutrophil/Lymphocyte ratio	4.85(0.48-13.48)	3.54(0.01-16.25)	0.138
CRP	111.71(11-366.46)	42 (3.17-128)	0.015

Mann-Whitney U test

Discussion

In this study of ours that evaluated the clinical and laboratory characteristics of adult patients with confirmed influenza-related lower respiratory tract infections, 50% of the patients were determined to be over 65 years of age. In the study of Çörtük et al., the mean age of influenza cases was 48.74±16.65, whereas it was 58.06±19.08 in our study [16]. The mean age of influenza A and B patients were found as 56.9 and 62.6 in our study. The mean age of patients hospitalized with the diagnosis of influenza A was 49.7±18.7 in the study of Gürgün et al., and 48.6±19.1 in the study of Özlü et al. [17, 18].

In our study, 53.3% of the patients in whom influenza was identified in lower respiratory tract samples were females and 46.7% were males that is similar to the study of Çörtük et al. [16]. When compared according to the distribution of types, female/male ratio was similar in influenza A cases (42.8% females/57.1% males), whereas the female ratio was higher in influenza type B (77.7% females/22.2% males). In the literature, the ratio of female and male in influenza A cases was similar to the ones in our results [17, 18]. In our study, 70% of influenza cases were type A and 30% type B. Previously done studies showed that influenza A cases were more frequent than influenza B cases that is similar to our results [16, 19, 20].

Most of the patients in our study group expressed complaints of fever, cough, and malaise. In the study published by Çörtük et al., the most frequently recorded symptoms were a cough (87%), fever (63%), and dyspnea (58.7%) [16]. When the symptom distribution according to the type was analyzed, symptoms were found to be similar in types A and B. Fever, cough, and malaise had similar rates in both type A and type B. In the study conducted by Sohn et al., cough, fever, and dyspnea were reported in 94.9%, 89.8%, and 62.7% of their influenza cases, respectively [21]. In the study of Özlü et al., cough was present with an incidence of 87.4%, fever 77.5%, dyspnea 76.8%, and sputum 61.5% in influenza A patients (19). Görgün et al. reported fever in all of their influenza A patients, cough in 95%, malaise in 90%, and myalgia in 85% [17]. In our study, myalgia was found to be present in 19% of the influenza A patients, 33.3% of the influenza B patients, and 23.3% when both groups were considered together. The retrospective characteristic of chart reviews might have led to the deficient recording of these symptoms.

Since it was a study involving adult patients, the effects of the current comorbidities on influenza infections were also evaluated. The presence of an additional disorder was identified in 66.7% of the influenza cases, and the most common ones were diseases that might have effects on the immune system such as DM and hematologic malignancies. The most frequent comorbidities in influenza A cases were hematologic malignancies with a rate of 28.5% and DM with a rate of 23.8%. In influenza B cases, DM was found to be present in 44.4% and hematologic malignancy in 11.1% of the patients. Görgün et al., in their study, reported a clinical condition that could have led to immune suppression in 30% of their patients with influenza A [17]. They reported their DM rate as 5% and cardiovascular disorder rate as 35%. Sohn et al. determined that their influenza A patients had comorbid diseases with a frequency of 59.2% Among these comorbidities, the most frequently met were neoplasms with a rate of 15.3%, cardiovascular disorders with a rate of 13.6%, and DM with a rate of 11.9%. Additionally, they stated that there was a history of corticosteroid or other immunosuppressive drug use in 25.4% of their patients [21]. In the study conducted by Jain et al., asthma was identified in 28%, obesity in 29%, and DM in 15% of influenza patients receiving inpatient treatment [22].

The radiological investigation is an essential diagnostic method in diagnosing pneumonia. In the great majority of our case group, Posteroanterior (PA) chest X-ray was obtained for a diagnostic purpose or for severity assessment of pneumonia; in only 6.7% of our patients, the radiologic assessment had not been performed. Radiologic infiltration was detected in 56.7% of our patients, whereas no infiltration was present in 36.7%. In the study of Sohn et al., the infiltration detection rate was 88.1% in influenza A patients [21]. In our study, the infiltration detection rates were similar in our comparison according to influenza subtypes. The detection rate of the radiological findings was 57.8% in influenza A and 66.6% in influenza B, and no statistical difference was determined between these two rates (p=0.493). In the study conducted by Kloth et al., it was also determined that the radiologic pattern had not changed according to the influenza subtypes [23]. In our study, the chest X-ray infiltration detection rates of patients with and without any additional disease that could have affected the immune system were similar (immune system affected patients 66.6% whereas unaffected patients 53.8%, p=0.488).

Kloth et al., in their study, described similar radiologic findings in computerized tomographic evaluations of influenza patients with and without immune suppression [23]. The comparison of laboratory parameters of the cases obtained by hemogram such as leukocyte, neutrophil, lymphocyte percentage, and the calculated neutrophil/lymphocyte ratio between the groups with and without radiologic infiltration did not reveal any sig-

nificant difference. However, a statistically significant relationship was found to be present between serum CRP level and the presence of infiltration on chest X-ray. The probability of infiltration presence increases on chest X-rays of the patients with elevated CRP levels. From a clinical practice point of view, this finding provides proof for requesting a radiologic investigation in patients with elevated serum CRP, regarding the diagnosis of influenza pneumonia and its need assessment for treatment. In various studies, it has been emphasized that CRP might be a prognostic indicator. In the study conducted by Morton et al., CRP values of early discharged in patients hospitalized with the diagnosis of influenza A were found to be significantly lower, compared to patients who had been discharged from the hospital later [24]. In the study of Qian et al., serum CRP level in patients followed up with the diagnosis of influenza A was shown to be higher in cases with clinical status resulting in mortality when compared to survivors. Also, Gao et al. reported that CRP levels were more elevated in cases with clinical features of influenza A and a fatal outcome when compared to survivors [25-26]. As in our study, this finding suggests that measurement of CRP level is important for identifying the patients who might develop complications of respiratory failure due to pneumonia. As a limitation, it is possible that since our study was conducted retrospectively, clinical symptoms might not have been adequately evaluated. The limited number of cases reduces the probability of our results to represent the entire population. For the development of recommendations regarding various risk groups, multi-centered studies with more patients need to be conducted.

For the development of standards regarding the management of influenza pneumonia in our country and recommendations in terms of good clinical practice, our results need to be supported by multi-centered studies having large patient series.

Conclusions

It was determined that in 66.7% of the cases with detected influenza virus in lower respiratory tract samples, additional diseases were present and the majority of these were disorders that had effects on the immune system such as DM and hematologic malignancies. This suggests that influenza virus can pass to the lower respiratory tract more easily in the presence of comorbidities affecting the immune system. This situation shows the importance of immunization particularly in this patient group. Symptoms of fever, cough, malaise were present in the majority of our patients. Influenza pneumonia should be kept in mind in patients with comorbidities presenting with the symptoms of fever and cough during the influenza season. Although radiologic assessment is not required in every case of influenza, CRP level was found to be associated with the presence of infiltration on chest X-ray in our study. This suggests that radiologic assessment may be required in patients with elevated CRP levels.

Scientific Responsibility Statement

The authors declare that they are responsible for the article's scientific content including study design, data collection, analysis and interpretation, writing, some of the main line, or all of the preparation and scientific review of the contents and approval of the final version of the article.

Animal and human rights statement

All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. No animal or human studies were carried out by the authors for this article.

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Conflict of interest

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